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PARONYCHIA OR PERIONYCHIA: AETIOLOGICAL ASPECTS.

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OVER the subject of inflammation of the nail fold, if text-books are any guide, there hangs an atmosphere of uncertainty and gloom. This may be the natural reaction to the light-hearted enthusiasm that colours much of the published work; and it is therefore with some trepidation that we venture into this shadowy territory. Our main excuse is that it is a common problem which we cannot well avoid.

CLINICAL FEATURES.

We think we can distinguish two types of paronychia.

Primary paronychia is characterized by an onset, which is often sudden, on one finger-nail fold, of swelling, redness, heat and tenderness. It is followed by similar changes in other nail folds and any number from one to all ten digits may subsequently be involved, though usually only a few are affected. In this series of 104 cases 42 showed only one digit affected, the rest multiple lesions averaging 3 per person. In a fully developed lesion the bolster swelling and pocket underneath are the pathognomonic features, with or without nail-plate damage. They tend to heal slowly but relapse is frequent.

Secondary paronychia.—The nail folds are thickened, obscuring the cuticle; there is no redness, and no sudden onset. The folds are merely participating in a low-grade chronic inflammatory condition of the skin of the fingers, as in degreasing dermatitis, atopic eczema, or psoriasis. In bacteriology and mycology these cases differ from the primary group and the infective element is minimal or non-existent. We recorded only 20 cases of this type. In 24 cultures for fungi we obtained no *Candida albicans*. *Staph. aureus* coagulase + was

grown on 4 occasions only. It is these cases—but only these— which give some support to the idea championed by Benedek (1954) that paronychia is no more than a " pompholyx of the nail organ ". We shall not discuss secondary paronychia further.

Onset and Course.

Most cases of paronychia persist for months or years, and the longest period recorded in our series is 35 years. The average for the series was 2 years.

The course is characterized by alternate flaring up and dying down of activity in one or more nail fold, one usually succeeding another. Careful questioning of patients will elicit the fact that the swelling of each finger-nail fold started quite suddenly, sometimes following injury but more often without any recollection of preceding damage. The distinction which we had visualized between acute paronychia and subacute or chronic cases began to lose its sharpness the further we enquired, until we concluded that there was a difference only of degree between the acute painful throbbing swellings with lymphangitis, lymphadenitis and fever, and the bolster swellings with pockets between fold and plate which are tender at times but more usually do not show those secondary severe effects. In general the *Staph. aureus* infections are more frequently responsible for acute and painful swelling, with a fairly rapid invasion of the fold and a tendency to burrow under the plate which may subsequently be shed or removed surgically ; whereas candida infections are seldom severe enough to cause shedding of the nail, and their invasion is slower with much milder symptoms. But in early lesions of a few days' duration it may be impossible to make any distinction on clinical grounds as to the infective agent, or to say with any certainty whether the condition is likely to resolve, or to persist and become chronic.

The question may well be asked what, if any, part does the infecting organism play in the production of the lesion. Several writers have held that the micro-organisms found are unimportant and are merely saprophytic in tissue already damaged by mechanical, chemical or biochemical means. But it is well accepted that injury and predisposition can pave the way for infection—e.g. " hang-nails " and puncture wounds may give rise to whitlows ; and minor damage to the horny layer was essential in Kligman's (1952) successful production of experimental scalp ringworm in children.

The opportunities for the study of early lesions, though few, have been sufficient to give some idea of the sequence of events.

The first patient, a woman aged 29, showed lesions varying from one day to ten days old. The earliest lesion on the left little finger was a delicate narrow yellow crescent corresponding exactly to the cuticle over the lunula. There was some redness and swelling of the fold, slight tenderness, but *no pocket*. (She attended because of the bolster swellings and pockets of older lesions on other fingers.)

Scraping this crescent readily broke through the thin covering of horny layer to yield a small quantity of yellow pus, which grew pure *Staph. aureus*, coagulase+. No candida were seen in films, and no candida grown, yet *Candida albicans* was grown in quantity from the right little finger fold which had been inflamed for several days. Subsequently *Staph. aureus* coagulase+ was grown in abundance from the left thumb fold and from the nose, but candida has been seen again quite recently in a relapsing fold lesion.

Another early lesion of 2 days' duration was seen in a child aged 5. This showed a narrow crescent of yellow colour with bolster swelling on the lateral fold of the left middle finger from which *Staph. aureus* coagulase+ was grown. There was also present an older lesion of 5 days' duration which had been incised and had yielded a

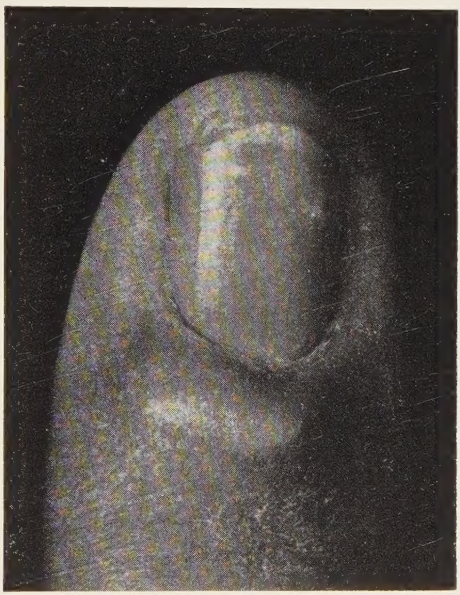

FIG. 1.

culture of *Staph. aureus* coagulase+. Repeated cultures have yielded no candida or other organism.

Whatever the primary infective agent in these two cases, *Staph. aureus* appeared to be early on the spot. But other cases have shown that *Candida albicans* can be the sole organism present even in the first two days and remain so apparently for months. Fig. 1 shows a two-day-old lesion on the right little finger, of different pattern from the first two cases, in a woman aged 55. Six other digits had been previously and similarly inflamed. There is a sizeable pustule, with shiny tense red swelling, but the cuticle is intact, still firmly attached to the nail plate. The pus contained fairly abundant thin long branching mycelium and the culture gave pure and profuse growth of *Candida albicans*. No other organisms were seen or grown. This patient's other nail-fold lesions had all started in this way with closed abscesses, and all subsequent cultures yielded nothing but *Candida albicans* pure and in abundance.

A fourth instance of an early lesion, of 7 days' duration, is very like the last. The woman aged 61 had had two other digits affected for 18 months which had slowly but not completely healed. The pustule was situated as in the last case, the cuticle

margin over the nail plate intact, and the skin proximal to the pustule swollen, shiny and red. On lifting off the lid we found the whole depth of the fold missing, the cavity going right back to the root of the nail. Whatever the agent the whole thickness of nail fold had been destroyed and only the intact nail plate remained to form the floor of the abscess. Cultures yielded 60 colonies of *Candida albicans*, but there was also a moderate growth of coliform bacilli.

The idea that *C. albicans* enters the nail-fold pocket and grows as a harmless saprophyte seems to us untenable in view of these and similar findings. At the onset a fully developed abscess is compatible with an apparently healthy and intact cuticle firmly attached to the nail plate and there is *no pocket*. The route of infection to this site is arguable. It could conceivably be blood borne ; but far more likely entry is through a minute invisible split or crack in the keratin of the cuticle overlying the nail plate. The pocket is formed later by the bolster-like swelling of the fold. This space between fold and plate may extend to the root.

The Seed.

Clinical and experimental evidence is steadily accumulating in favour of candida's role in paronychia. There is the frequent presence of candida in the paronychial lesions, a point that one need not labour because it is so well known (Hellier, 1955 ; Whittle, 1955 ; Drouhet, 1957 ; Alkiewicz, 1957). Frain-Bell (1957) found 70% of his cases yielded *Candida albicans* in culture, and Marten (1958) finds that candida can be recovered from practically all cases of chronic paronychia. Our figures fall considerably short of this, partly because we included in our series early cases in which *Staph. aureus* was often the only organism recoverable, though candida is still numerically far the most important organism seen (Table I). But more than its mere presence in lesions, and absence in healthy nail folds, is required to establish its pathogenicity, and it is in the experimental field that further evidence has been adduced. Vilanova (1956) and his colleagues have succeeded in provoking a mild but definite paronychia by the continued application of a suspension of live *Candida albicans* to the healthy nail fold. More recently Kapica and Blank (1957) have shown that *Candida albicans* can break down keratin *in vitro*, and from it derive all its nitrogen requirements, with liberation of amino-acids similar to those obtained by Blackburn (1950) in the hydrolysis of wool, and by Daniels (1953) in the breakdown of human hair by *M. canis* ; Rothman (1953) describes in some detail the enzymatic digestion of keratin by pathogenic fungi.

The Soil.

Maceration.—How readily candida can gain a footing in the macerated nail fold is shown by the following experiment.

A normal left middle finger-nail fold was scraped gently and the scrapings sown on Sabouraud's medium. The culture remained sterile. The finger tip, including

TABLE I.—*Paronychia—Mycology and Bacteriology.*

		Cases.	Isolates.
Fungi	*Candida albicans*	41	56
	Candida—Other species*	20	31
	Candida—All species	61	87
	Total	104	147 cult.
Bacteria	*Staph. aureus* (coag. +)	11	16
	Coliform bacilli	6	6
	Ps. pyocyanea	3	3
	Strep. haemolyticus	2	2
	Total	22	52 cult.

* This includes *C. parapsilosis* (15), *C. tropicalis* (3), *C. krusei* (1), *C. guilliermondi* (2), unspecified candida (10).

nail and nail fold, was covered with waterproof adhesive tape to seal off the fold, which was thus kept occluded continuously, the tape being changed when damaged or dirty at intervals of three or four days. When the fold had been so occluded for 13 days a further culture was taken from the now macerated fold. This culture also remained sterile. The macerating process was continued and after 21 days' occlusion scrapings from the fold showed yeast-like bodies in abundance and cultures gave about 50 colonies of *Candida guilliermondi* on a slope. Similar results were obtained by covering the right middle finger fold and in this case the effects were noted after only 7 days when about 30 colonies of candida were recovered. There was no sign of paronychia or perionychial inflammation during the four weeks of observation, so that the mere presence of candida, even in abundance and particularly in its yeast phase, affords no evidence of invasive power or pathogenicity. In these macerated folds we were unable after 21 days to find a trace of mycelium, whereas we frequently find mycelial threads in quantity in the scrapings from the inflamed folds in paronychia.

Indirect predisposing factors.—The difficulty experienced by Vilanova *et al.* in producing persistent lesions in the nail fold by applying live candida to it illustrates the importance of the soil. The maceration already mentioned, the age of the skin, and defects of circulation in the finger tips probably all play a part, though in such a small sample as ours it is impossible to prove any of these statistically. There are, however, certain indications ; Fig. 2 shows a peak age incidence in the fifth decade, and the fifth and sixth decades include no less than 50% of the cases, all females except four. These figures agree closely with Frain-Bell's taken from a much larger series. The overwhelming preponderance in women may not be world-wide and seems to be preventable ; in the United States of America, where much of the washing of dishes and clothes is done by machinery, the disorder appears to be less common.

Circulatory disturbances which have been mentioned by previous workers were noted in only 28 cases in our series (Table II) and this low incidence may perhaps give an indication of the infrequency with which obvious defects of circulation occur.

Trauma.—Injury when it is sudden is noted and is obviously important. Less obvious but probably no less important are the repeated injuries listed in Table II. Thimble-wearing may be the trauma that decides which digit is the

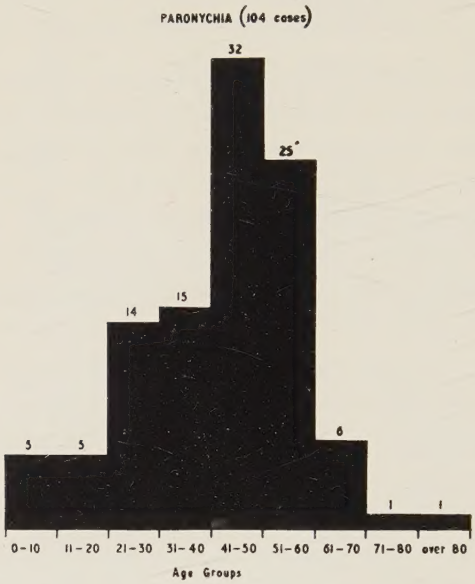

FIG. 2.

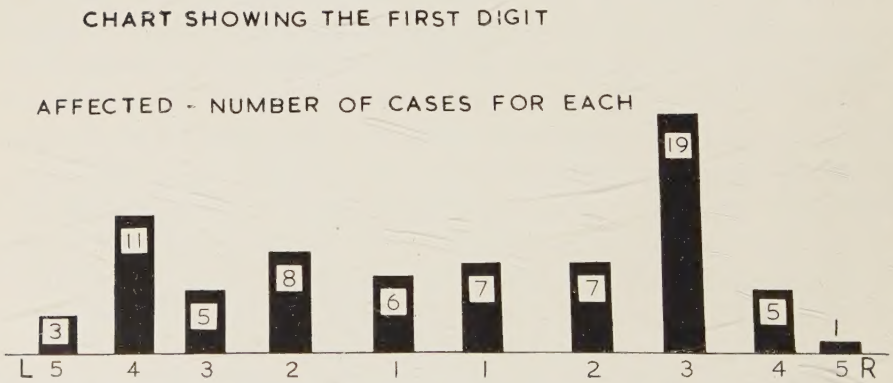

FIG. 3.—Showing the *first* digit to be affected, and the number of cases in which this occurs. Statistically the only significant figure is the figure 19 for the *right middle finger*, and this is highly significant.

first one to be affected, but in two women, one left-handed, no thimbles were worn, and the statistically significant predominance of the right middle finger as the *first* to be affected is probably due to its greater length and its greater liability therefore to trauma (Fig. 3). Frain-Bell found the right middle finger to be the one most *frequently* affected. The left middle finger probably suffers

less wear and tear than the right, except of course in left-handed subjects. Thimble-wearing is a dying habit, as many of us know to our cost.

TABLE II.—*Likely Contributing Factors in Primary Paronychia* (104 *Cases*)

Indirect	Sex	Female	97 cases
		Male	7 cases
	Age	50% (57 cases) in 5th and 6th decade	
	Circulatory disturbances	1. Hyperidrosis 2. Chilblains 3. " Dead fingers " 4. Arthritis of fingers 5. Constriction from wedding ring	28 cases
* Direct (trauma)	1. Wet and/or rough work		89 cases
	2. ? Thimble (starting on this finger)		17 cases
	3. Blow, crush, splinter, puncture wound, " hang nail "		15 cases
	4. Drastic manicure to nail folds		11 cases
	5. Biting, picking, scratching, rubbing		6 cases

* Note : There is some overlapping in these figures when more than one factor was recorded.

COURSE.

Under treatment the nail folds improved though, in many, progress was slow intermittent and incomplete, and relapse frequent.

Nail-plate involvement.—Fifty-eight of 104 cases showed some degree of damage to the plate which varied from mild roughening, through dirty green discoloration to gross disorganization with breaking up of the laminae, and

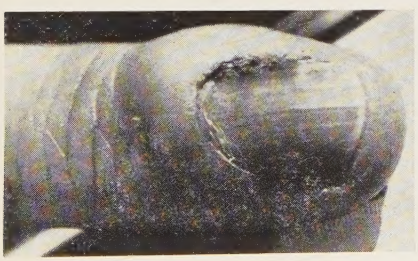

FIG. 4.

FIG. 5.

separation, in a few cases, of the plate from the bed. The splitting noted by Alkiewicz (1957) was infrequently seen. The frequent roughening and discoloration was usually confined to one side corresponding to that portion of the fold affected (Figs. 4 and 5). Candida can often be seen in the scrapings from the damaged plate but cultures are scanty, suggesting that the fungus is dying or dead (Figs. 6 and 7). The nail changes are unimportant, except cosmetically, because the active damage is taking place at the nail fold over the matrix of

the newly forming nail. As soon as the fold heals, new healthy nail forms, but it is of course six months before it reaches its normal length.

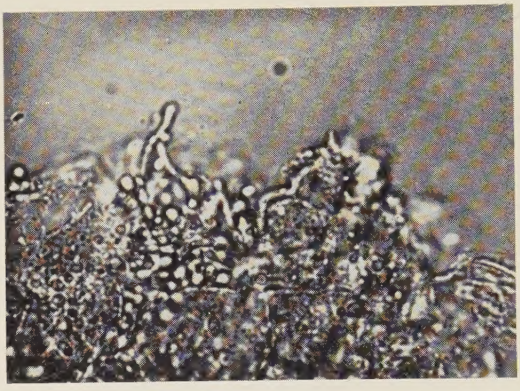

FIG. 6.—Nail *fold* scrapings from paronychia with mycelial elements present (potash mount). Slope cultures gave 100 colonies of *Candida albicans*.

FIG. 7.—Scrapings from the same nail *plate*, which was grossly damaged and infected. Note the thick-set mass of yeast-like spores ; which are mostly dead. Slope cultures gave only 4 colonies of candida.

TREATMENT.

The chief and by far the most important measure is to protect the fingers from wet and rough work. This may be achieved by avoidance, barrier creams (only partly successful) and rubber gloves preferably lined with cotton or suede. Local applications have included varnishes, paints, and creams with or without antibiotics, including Nystatin. We have so far made no systematic assessment of the effects of medical or surgical treatment. Since the nail changes are essentially secondary, we believe it is quite unnecessary to treat the damaged or infected nail *plates* as the French do (e.g. Drouhet) with abrasion and fungi-

cides ; candida infection behaves quite differently from trichophyton infection, which is a very much more serious problem.

Prognosis.

On treatment to date the prognosis is only fair. Fifty-two of our 104 patients were seen to be, or reported that they were completely free of their disability. Some of them may, of course, relapse. Thirty-five cases showed some paronychia persisting at their last attendance ; 17 were not traced.

Thirty-five years was the longest history. The average was $1\frac{1}{2}$ years for those that recovered, and 3 years for those still showing activity.

Discussion.

Evidence has been brought forward in support of the thesis that candida, though it may be associated with other organisms, is the most important infecting organism in chronic paronychia. We believe that it reaches the nail fold from without and can invade the fold if and when conditions become favourable. Maceration is clearly one condition. Candida can spontaneously colonize a macerated but otherwise healthy nail fold with great ease, as is exemplified by the experiment described above wherein occluding the fold with adhesive tape for a week or so was sufficient to allow the few spores, undetectable by culture, to germinate and yield an abundant growth in a second culture taken from the fold. There was no evidence of inflammation and only yeast forms were found. The mere presence of the fungus and its multiplication in a macerated nail fold is not enough, and other factors must be present for inflammation to occur. Injury is without doubt important. It may be a single, sudden and violent incident, and therefore remembered ; more often it is mild, repeated and unnoticed, as in housewives who are constantly damaging their finger tips, as well as macerating the folds, in the course of their housework. Around the menopause is the peak age incidence, a time at which general disturbances of circulation are common, and circulatory disturbances in the fingers were noted in 28 of our 104 cases. Ageing of the skin would hardly account for over 50% of the cases starting in the fifth and sixth decades. There may be other explanations, for instance endocrine action direct on the tissues. But we must admit that there is still an unknown factor which must be present if invasion is to occur.

The vagina seldom appears to be infected with candida (only 1 in 18 of our cases). But candida is often associated in paronychia with other organisms, particularly those which, like candida, (Raubitschek, 1947 ; Ormsby and Montgomery, 1954 ; Marten, 1958*a*) are commonly present in the alimentary tract ; this is almost certainly the reservoir of infection. Marten has shown the close association between organisms found in the nail fold in paronychia and

those in the gut. The same type of proteus appeared in nail fold and gut in 10 of 12 cases in which typing was carried out. The astonishing degree of contamination of the fingers that normally accompanies the daily emptying of bladder and rectum has long been known and has stirred public health officers into a campaign for greater cleanliness. Our figures have shown that there is a statistically significant numerical preponderance of the right middle finger over all other digits in being the *first* to be affected, and it is also the finger most likely, at least in right-handed subjects, to be contaminated after defaecation, though other digits may not escape.

It may be that in this way a highly invasive strain of candida reaches the nail fold, or alternatively the invasiveness of a comparatively harmless strain is enhanced by local conditions which favour its growth into, and destruction of, nail-fold tissue. Our frequent finding in paronychia of candida in the form of thin mycelial threads, and the appearance of this phase in keratin breakdown by candida in the published experiments mentioned above suggest to us that the fungus, in order to invade, may require conditions which allow it to develop mycelium. Mycelial formation in keratin takes time, probably at least 30 days under experimental conditions (Kapica and Blank). Further investigations which are under way may confirm or refute this view.

In putting candida first we may have underrated the aetiological significance of such organisms as *Staph. aureus*, *E. coli*, *Proteus* and *Ps. pyocyanea* which are less constantly found. The growth of candida may, by opening spaces in the keratin or changing the pH or oxygen tension, encourage the growth of these organisms ; or they in turn may enhance the invasive power of candida. Further study along these lines is needed.

Summary and Conclusions.

One hundred and four cases of primary paronychia have been reviewed.

Candida albicans was the predominating organism recovered.

Lesions in the early acute stage showed that the characteristic pocket that forms between nail and fold follows, and does not precede, invasion by the organisms.

The disease affected women in 96 of 104 cases.

Fifty per cent. were between 40 and 60 years old.

The right middle finger was most frequently the *first* digit to be affected. This is statistically significant.

Experimental occlusion and maceration for three weeks of a healthy nail fold gave rise to spontaneous active colonization of the keratin by candida.

The aetiology of paronychia is discussed ; the suggestion is put forward that candida is pathogenic and can invade the nail fold, but that its power to invade may depend on its change from the yeast to the mycelial phase.

Technique.

Scrapings from nail folds were examined in caustic potash and at the same time sown direct on tellurite Sabouraud beer-wort agar slopes. For the bacteriology a sterile swab moistened with saline was used.

Acknowledgments.

We wish to thank Dr. Jacqueline Walker of the London School of Hygiene for identification of all the fungus cultures submitted, Dr. M. H. Gleeson-White of the Department of Pathology, Cambridge University, for the bacteriology, and Mr. R. G. Carpenter, Statistician to the University Department of Human Ecology, for his statistical evaluation of the figures quoted.

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LIPOID DERMATO-ARTHRITIS (RETICULOHISTIOCYTOSIS).

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LIPOID dermato-arthritis is a rare disease resembling rheumatoid arthritis in which there is a profusion and dissemination of nodules unknown in the latter and the erythrocyte sedimentation rate is seldom much raised. Both the skin and the synovial membranes are involved in a histiocytic reaction including characteristic multinucleate giant cells with foam-free cytoplasm.

REVIEW OF REPORTED CASES.

The first case was described by Targett (1897), but the first detailed report was made in 1937 by Parkes Weber and Freudenthal. Their patient, a man aged 35, was crippled by "rheumatoid arthritis" and developed nodules on his hands, arms, trunk and head, swellings of the sheaths of the extensor tendons at the wrists and plaques over the shoulders. In spite of severe arthritis and slight fever the E.S.R. was "not decidedly accelerated". The histopathology of the nodules was not that of the necrobiosis which would be expected in rheumatoid arthritis; instead, the normal collagen bundles were separated by an infiltrate containing giant cells having from three to five or more nuclei. In spite of their resemblance to xanthoma cells, no definite fat could be demonstrated within them. They were named "pre-xanthoma cells" in the belief that they represented a transition towards true xanthoma cells, since faint, even sudanophil staining was visible in some of them. Freudenthal thought that they might be mature cells infiltrated with a special lipoid and pointed out their resemblance to Gaucher cells. The patient had a mild hypercholesterolaemia (230–350 mg.%) which returned to 110-140 mg.% when he had been on a low fat diet. Hypercholesterolaemia has not been a feature of subsequent cases. The patient's rheumatism and nodules improved and he was working as a night watchman 6 years after the onset, impeded rather than incapacitated by his disease.

Eighteen cases of this disease have been recorded, six in men and twelve in women (Targett, 1897; Weber and Freudenthal, 1937; Portugal *et al.*, 1944; Allington, 1950; Caro and Senear, 1952, two cases; Laymon, 1952; Montgomery, 1952, two cases; Goltz and Laymon, 1954; Davis and Wood, 1955; Kierland, 1955; Johnson and Tilden, 1957; Lapière *et al.*, 1957; Warin *et al.*, 1957, four cases). We have not included the case described by Graham and Stansfeld (1946) in spite of its close clinical resemblance, because

the giant cells were mononuclear and had foamy cytoplasm. We have excluded also the case of Montgomery and O'Leary (1934) as arthritis was absent and Nissl's granules were present in the cytoplasm of the giant cells. Layani's unique case (1939) had xanthomatosis with destructive arthritis.

The eruption consists of nodules on the fingers, the larger collecting about the joints, the smaller having a special affinity for the periungual region. The nodules are dermal and are seldom highly coloured. They do not ulcerate, but may bleed. They are frequently tender, sometimes painful and are occasionally itchy. The head is the next most common site, especially about the ears and nose. The mucosae may be involved as far as the larynx. Any region of the skin may be affected, but lesions below the knees are most uncommon. On the trunk, especially over the shoulders, iliac crests and sacrum, large soft swellings occur which seem to arise in relation to heat and pressure. Miliary lesions also occur and like the larger nodules tend to wax and wane and to disappear without trace. Atrophy following involution of nodules is very rare. Erythema in sheets, with or without papules or nodules, and linear and follicular lesions occur. Xanthelasma palpebrarum, typical in clinical and histological form, is common. Soft, fluctuant swellings form on tendon sheaths, especially at the wrists. There is a general resemblance to the eruption of xanthomatosis and in distinguishing between the two diseases clinically we would emphasize in the latter the yellow colour, the occurrence of lesions on the heels and the familial incidence. All the cases of lipoid dermato-arthritis have been sporadic.

The joints ache and are restricted more in active than passive movement. Any joint can be affected, including the temporo-mandibular and spinal. The terminal inter-phalangeal joints are especially susceptible. Swellings of the joints are usually due more to synovial thickening than to obvious effusion. The process spreads from the synovium to the adjacent bone which is destroyed without any osseous reaction being visible radiographically. The carpal phalanges melt away and the fingers become shortened and fleshy, a state to which the term *main en lorgnette* has been applied (Marie and Léri, 1913) because the fingers can be elongated and compressed like a telescope. Healing by ankylosis is most exceptional and the mobility of the joints is often increased.

Severe cases develop pyrexia, loss of weight and muscular weakness, but the E.S.R. is seldom much raised. Enlargement of the liver, spleen and lymph glands is unusual. Three patients have died, one of secondary carcinoma of the colon, one with occult malignant growth in bronchial lymph glands without a known primary tumour, and one of the disease alone. In the last two cases there was terminal pericarditis. Giant cells have been found diffusely scattered throughout the dermis, subcutaneous tissue, lymph glands and endocardium.

The course of the illness is long, the skin lesions tending to fluctuate and then to clear. The rheumatism persists longer, but the disease burns itself out in time. The age of onset bears some relation to the severity of the disease, for the three cases which started before 30 are incapacitated. On the other hand, onset at 50 is no guarantee of mildness, as this was the age of onset of two who succumbed to the disease.

Treatment of every sort has proved ineffective and heat harmful. The arthritis does not respond to steroid therapy.

The cause of the disease is unknown. There is no inherited predisposition and no racial susceptibility ; one patient was Japanese, one Red Indian, one Brazilian, one Belgian, seven British and the remainder American. Two had thyroid disease, one being hyper- and the other hypothyroid at the onset. One developed the disease while convalescing from colectomy performed for a growth and died of secondaries after his skin nodules had disappeared.

The histopathology of the skin lesions is that of a non-encapsulated but defined dermal tumour in which histiocytes and giant cells, mixed in varied proportions, displace the normal collagen bundles without provoking any significant reaction. The overlying epidermis is stretched and thinned in contrast to the hypertrophy seen in myoblastoma. The giant cells have three to five or more nuclei, not arranged in any particular fashion and homogeneous or finely granular but never foamy cytoplasm devoid of droplets of fat, but which sometimes gives a diffuse, pale colour with fat stains. Portugal *et al.* (1944) showed that the giant cells would take up injected lipoid, and Caro and Senear (1952) that they would take up iron from injected iron saccharate solution. Warin (1953) observed that the synovial membranes contained the characteristic giant cells, and Goltz and Laymon (1954) confirmed this. Warin *et al.* (1957) thought that the giant cells contained a lipoid-polypeptide complex because mild acid hydrolysis increased their sudanophilia. Montgomery *et al.* (1958) suspected the presence of lipofuscins.

Solitary lesions occur in patients without rheumatism (Zak, 1950 ; Purvis and Helwig, 1954) and it has been supposed that this is an abortive form of the disease ; but Davis and Wood (1955) doubt this since the solitary lesions have a different histopathology. There is a more intense inflammatory reaction, the giant cells are larger, have fewer nuclei and their cytoplasm is sometimes foamy and contains fat droplets.

The nomenclature is complicated. Authors have found four chief ideas to convey viz., the presence of giant cells, the resemblance to xanthoma, the histopathological resemblance to histiocytoma and the involvement of the skin and synovial membranes by the same process. The name with the greatest influence has been " reticulohistiocytoma " given by Caro and Senear, but this perhaps hints at a malignant process, and " reticulohistiocytosis " and " reticulohistiocytic granuloma " have been suggested as alternatives. Warin *et al.*

(1957) put forward "lipoid dermato-arthritis" which Parkes Weber (1957) supported and this name has the virtue of not suggesting involvement of the reticulo-endothelial system, for which there is insufficient evidence. Davis and Wood (1955) recommend restricting "reticulohistiocytic granuloma" to the solitary lesions, and using "reticulohistiocytosis" for the disease under discussion.

Case Report.

A married woman, aged 56. She has never enjoyed perfect health.

At the age of 50, she was investigated in a gynaecological ward and a radium menopause was induced. A polyp was removed from the cervix uteri, and was found

Fig. 1.

histologically to be benign and typical. At this time the patient had multiple complaints including long-standing backache, habitual constipation, heartburn, sickness, shortness of breath, ankle swelling, rheumatism, cough with some sputum, frontal headaches and giddy turns. She had recently been investigated at a chest clinic on account of pleural pain and slight haemoptysis. Physical examination had failed to reveal any disease and there were no skin nodules. Her mother, four sisters and a brother were alive and well. Her only other sibling, a sister, had died from tuberculosis of the bowel, and her father had died of carcinoma of the bronchus.

She first came to our attention two years later on account of a profuse crop of nodules on her fingers and hands and exacerbation of her rheumatism.

The nodules (Fig. 1), which she had noticed for 9 months, were mostly on the backs and sides of the fingers and the palms were free. The larger nodules, about 1 cm. in diameter, were near joints and many of the smaller, from 1 to 2 mm. in diameter, were clustered around the nails like rows of coral beads (Fig. 2). The larger nodules were plum-coloured when she was seen in the out-patient department, but when she was at rest in bed they faded to match the normal skin. When compressed between

the finger and thumb they felt rubbery, but when pressed against bone they felt hard. The nodules were obviously dermal but she said that they bled, and slight bleeding was observed once.

Her joints had ached and been stiff for many years and in the last four years she had received physiotherapy without success. The pain spread from the feet and ankles, fingers and wrists to her knees, elbows and shoulders. The pain was out of proportion to the physical signs of slight limitation of movement and creaking. Transient swellings of ankles and knees were observed, but never any effusion or redness. Her fingers were deformed by the nodules, but there was no ulnar deviation of fingers or hands.

She had been wheezy for at least 6 years and had had three episodes of pleural pain with blood-streaked sputum. On examination, expiration was prolonged and wheezy on occasion and there were often rhonchi ; her sputum was tenacious and small in amount and on microscopy was seen to contain squames, pus cells and gram positive cocci, which proved to be pneumococci. A skiagram of her chest showed

Fig. 2.

ill-defined opacities in the lower zones with fine linear densities which have remained constant for two years and resemble peri-bronchial lymphatic permeation (Dr. A. M. Stewart). A Mantoux test at 1 in 1000 was positive.

She had typical xanthelasma palpebrarum of both upper eyelids but no sign of cardio-vascular disease, and repeated electrocardiograms were normal. The peripheral blood and sternal marrow were normal on repeated examination. The urinary 17-ketosteroid excretion (one estimation) was low (3·6 mg. per 24 hours).

During two years of observation, the disease has fluctuated in severity, and she is now better. Wax baths made the nodules softer and prone to bleed and rest in bed caused them to shrink. New nodules appeared on her ears and nasal septum and soft painless swellings of the extensor tendon sheaths at the wrists came and went in a matter of months. The range of movement of the joints has always been good. The E.S.R. has remained at 2 or 3 mm. 1 hr., until the last reading of 15 when paradoxically she was much better. Small erosions have appeared radiologically in the bones of the hands near the inter-phalangeal joints in sites corresponding to the nodules.

Treatment has been ineffective, with the exception of rest in bed in hospital. At first we diagnosed Kaposi's sarcoma and she received 13·5 mega units of penicillin by injection over 16 days, followed by X-irradiation of one thumb, and then a course of nitrogen mustard analogue, C. B.1348 (Dr. E. F. Ridley). For the year since the correct diagnosis was made she has been on a low fat diet (12 g. per day) and blood cholesterol levels have been 275, 225 and 245 mg.%.

Investigations.

Examination of serum lipids by electrophoresis (Dr. H. Thom). 40 μl. of serum were examined by paper electrophoresis (Whatman No. 1 paper; barbiturate buffer pH 8·6). After drying, the papers were stained with Sudan black for lipids. Three main lipid bands appear, "alpha lipid" usually located with alpha-one globulins, "beta lipid" with beta globulins, and "omega lipid" which is the stained area around the origin. For quantitative estimation of the lipid fractions, standard quantities of arachis oil were applied to the dried strips and stained with the serum lipids. The relative intensities of the dyed bands were estimated by photo-electric scanning.

13.iv.58, morning specimen of serum: The alpha lipid band was more intensely stained than that of the "normal" serum sent as control. The beta lipid band was very much more intensely stained than that of the "normal" serum.

27.v.58, early afternoon serum specimens:

	Patient. (mg. %.)	"Normal." (mg. %.)
alpha lipid	195	205
beta lipid	665	695
omega lipid	95	80
phospholipid P	9·2	8·7

Histopathology.—Biopsies of five nodules showed non-encapsulated but moderately circumscribed dermal tumours composed of histiocytes, giant cells and many blood vessels, separating normal collagen bundles. Polymorphonuclear leucocytes were never observed and there were only occasional lymphocytes. Giant cells were seen in varied amounts in the five specimens. They varied in shape and size, ranging from 30 to 60 μ in diameter. Their borders were not always well defined. Their cytoplasm was most frequently eosinophilic, sometimes with basophilic streaks and smudges and was either homogeneous or finely granular, but never foamy. They contained up to 15 nuclei, which were irregularly distributed within the cell. The nuclei varied in their degree of basophilia, which was generally quite intense, but sometimes less marked, when the nuclear structure and the nucleoli were more clearly visible.

This is a typical mild case of the disease. An unusual feature is the involvement of the chest. Montgomery's (1952) second case, in a woman of 24, had multiple pulmonary nodules, and two fatal cases of Warin *et al.* (1957) showed involvement of the hilar lymph glands. With regard to the quantity of the giant cells in the biopsy material, other authors have noticed variation of this sort in successive biopsies taken from the same patient, some having a preponderance and others a minority of giant cells.

Histochemical Investigations.

The object of the following investigations was to elucidate the chemical nature of the cytoplasm of the multinucleate giant cells.

Methods and Results.

Biopsy specimens were fixed in 10% neutral formalin.

Treatment of frozen sections with Sudan IV in 70% propylene glycol resulted in rather diffuse dyeing of the cytoplasm, suggesting that the sudanophilic material was in a finely dispersed state. The degree of sudanophilia was not enhanced by

preliminary mild acid hydrolysis in 10% acetic acid for 1 hour at 37° C. Treatment of frozen sections by the Schultz reaction for cholesterol and cholesterol esters gave a negative result and no birefringence was observed in unstained frozen sections under the polarizing microscope. Formalin-fixed tissue, which had been post-chromed for about 30 hours in 3% potassium dichromate, was embedded in paraffin and sections were treated with Sudan black B. This resulted in a brownish-black coloration of the cytoplasm similar in appearance and distribution to the orange coloration of Sudan IV.

The periodic acid-Schiff technique (PAS) on formalin-fixed paraffin-embedded sections gave a positive reaction in the giant cells, which was not evenly distributed, but often most at the centre or to one side of the cells. Incubation of sections in malt diastase 0·1% in buffer of pH 4·6 for 1 hour at 37° C. or in salivary diastase in glass-distilled water did not alter the intensity of the PAS reaction in the giant cells, but obliterated the reaction given by the cells of the sweat gland acini. The PAS reaction was blocked by acetylation. The combined dialysed iron and PAS method resulted in purple coloration of the cytoplasm identical in distribution with the PAS reaction alone. No metachromasia was produced in the cells by treatment of sections with toluidine blue or with Alcian blue.

Perl's method for ferric iron gave a positive Prussian blue reaction, as granules in the cytoplasm of many of the larger histiocytes and in some cases a faint blue coloration in the cytoplasm of the multinucleate giant cells.

The coupled tetrazonium reaction with benzoylation for tyrosine, tryptophan and histidine was negative, but the Millon reaction for tyrosine occasionally produced a faint orange colour in the cytoplasm.

TABLE I.—*Histochemical Findings.*

Test.	Frozen (F.) or Paraffin (P.).	Result.	Significance.
Sudan IV	F.	+ faint	Lipid, no neutral fats.
Sudan IV following mild acid hydrolysis	F.	Not enhanced	Not lipid-polypeptide.
Sudan IV following incubation in papain	F.	„	Not lipid-protein.
Sudan black B	F. and (post-chromed) P.	+ (brown-black)	Lipid / lipoprotein / phospholipid.
PAS	F. and P.	+ (red to purple-red)	Polysaccharide (P.).
PAS following acetylation	P.	—	1 : 2 glycol groups.
PAS following diastase	P.	+	Not glycogen.
PAS following acetone extraction	Formalin fixed P. and F.	—	Glycolipid, phospholipid or unsaturated lipid.
Baker's acid haematein	P.	—	No phospholipid.
Colloidal Fe PAS	P.	+ (purple)	Possibly mucoprotein.
Metachromasia	F. and P.	—	No acid mucopolysaccharide.
Birefringence	F.	—	No cholesterol, chol. esters or crystalline fats.
Schultz	F.	—	Cholesterol and esters absent.
Perl's Prussian blue reaction	P.	± diffuse (faint)	? Iron.
Millon	P.	± (faint)	? Tyrosine present.
Coupled tetrazonium after benzoylation	P.	—	Tyrosine, tryptophan and histidine absent.
Schmorl	P.	+	Lipofuscins, melanin, etc.
Long Ziehl-Neelsen	P.	+ (pink)	? Lipoprotein.
Methylene blue extinction	P.	< pH 4·2	Lipid components/acid mucopolysaccharides.

The binding capacity of the giant-cell cytoplasm for methylene blue at various hydrogen ion concentrations was compared visually following immersion of sections in buffered methylene blue solutions. Virtual extinction of methylene blue staining occurred at and below pH 4·2.

Schmorl's potassium ferricyanide method gave a blue colour in the cytoplasm and the long Ziehl-Neelsen method a pink coloration, tending to mauve if nuclear counterstaining was excessive. The coloration was evenly distributed throughout the cytoplasm by both of these methods.

Significance of the Results.

The finely-dispersed, faint sudanophilia of the cytoplasm of the multinucleate giant cells has been recorded in many cases and Montgomery *et al.* (1958) also showed a positive reaction to Sudan black B. We failed to observe any increase in the degree or extent of sudanophilia following mild acid hydrolysis in contrast to the findings of Warin *et al.* (1957).

Our result with the PAS reaction was always positive but the end-product varied from pink to purple-red and we think it may have been due to the 1 : 2 glycol groupings in mucoproteins (or glycoproteins), or to glycolipids. The colloidal iron and PAS reaction may have been due to the presence of mucoprotein.

The Prussian blue reaction was applied because Case 1 of Caro and Senear (1952) showed an increase in the iron content of the tissue by micro-incineration methods, although a positive reaction had not been obtained histologically in the multinucleate cells. We found the histiocytes to be generally rich in iron, which may have been due to leakage from blood vessels and indeed bleeding had been observed clinically. Our patient had no connection with metal-working as had that of Caro and Senear.

The extinction of the cytoplasmic binding capacity for methylene blue at and below pH 4·2 may indicate the presence of glycolipid or mucoprotein and in the absence of demonstrable metachromasia the extinction at that hydrogen-ion concentration could not be due to mucopolysaccharides.

Montgomery *et al.* (1958) suggested that the positive reactions which they found in the cytoplasm of the multinucleate cells were due to the presence of a type of lipofuscin. We found the Schmorl reaction positive, but the long Ziehl-Neelsen method negative for acid-fast lipofuscins. The pink colour produced could be due to lipoprotein.

It must be conceded that although some protein may be present in the giant-cell cytoplasm we were unable to show this satisfactorily and in only some sections subjected to the Millon reaction the cells showed a faintly positive result.

We have shown that the cytoplasm of the multinucleate giant cells definitely includes a molecule containing a 1 : 2 glycol group, a lipid component and perhaps some demonstrable protein. We think that the 1 : 2 glycol groups may

be derived from polysaccharide molecules, which could be conjugated either with lipid as glycolipid or with protein as glycoprotein. The very faint reaction for protein suggests that protein may be present in a combined form, for example a lipoprotein, or glycolipid adsorbed to protein. In order to clarify this issue an attempt was made to unmask any lipid combined with protein by incubation of frozen sections in papain solution followed by Sudan IV treatment. No increase in sudanophilia was observed. Formalin-fixed tissue (no fresh tissue being then available) was extracted with hot acetone and submitted to the PAS technique when all PAS positive material was found to have disappeared from the giant cells. From these observations we conclude that the PAS positive material consists of glycolipid or phospholipid. By the foregoing methods it is not possible to differentiate between them (Pearse, 1953). Material which had already been fixed in formalin was placed in neutral formol-calcium for 12 hours and submitted to Baker's acid haematein method. No positive material was demonstrable in the giant-cell cytoplasm and it was concluded that no phospholipid or unsaturated lipid was present.

At the beginning of this paper we mentioned Freudenthal's idea that the "pre-xanthoma cells" might contain some special lipoid. In 1955 Parkes Weber wrote: "On the whole I suggest that the case of Freudenthal and Weber was a new syndrome of a rheumatoid condition combined with a metabolic lipoid disorder in which the accumulating lipoid was of somewhat similar nature to the kerasin of Gaucher cells". It is of interest that kerasin is a glycolipid and we have shown that the lipid material in the giant cells in our case is also a glycolipid.

Our conclusion leads us to support Warin *et al.* (1957) in the use of the name of lipoid dermato-arthritis which they chose for this disease.

Summary.

Lipoid dermato-arthritis has been defined with particular reference to the giant cells which have a foam-free cytoplasm.

The reports of the eighteen published cases have been combined into a review of the disease.

The suggestion of Davis and Wood (1955) that patients with solitary lesions have a different disease is accepted.

A typical mild case with suspected pulmonary involvement has been described.

Histochemical studies showed that the giant cells contain a glycolipid.

The name lipoid dermato-arthritis (Warin *et al.*, 1957) is preferred to reticulohistiocytosis.

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OCCUPATIONAL DERMATITIS.

Its Prevention, with Special Reference to Barrier Substances.

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Theoretical Considerations.

Although much has been written in the medical and cosmetic trade press on the formulation and effectiveness of barrier substances, very little has been of constructive value. There has been a recent change in the trend of medical opinion and it is now widely thought that barrier substances serve little or no useful purpose in the prevention of dermatitis in industry, or that their usefulness is almost entirely psychological and of benefit to a minority. With this background of opinion, I started to study the reactions and effectiveness of a selection of the more common barrier substances currently marketed, with special reference to their use in the leather industry. Subsequently, investigations were made into other methods of protection.

The required property of a barrier substance is generally agreed to be that of forming around the exposed parts of the hands and forearms an invisible glove which should be flexible and prevent contact between the irritant and the skin. How the barrier should achieve this is not so readily agreed. A view still held by the majority of manufacturers of barrier creams is that the main consideration is to block the surface cone of the hair follicle with some inert absorbent. A soap is added to facilitate its easy removal by washing, a wax to render it water-resistant and a little grease to keep the skin supple. A large number of marketed creams have been no more scientifically prepared and even the more complex creams have deviated only slightly from this basic formula.

The idea of blocking the follicles is fallacious and even potentially dangerous. The follicles are important only where they have lost their hairs. In normal circumstances, the space between the follicle wall and the hair is extremely small and even if the cavity were completely void it would allow only a small amount of irritant to penetrate. In addition, the natural secretion of grease is sufficient to protect these spaces and a strong solvent would be required to remove it in a normal working period.

The most effective factor in the prevention of dermatitis is undoubtedly the maintenance of the stratum corneum. This is thickest and most resistant on the palms and soles where industrial dermatitis is exceptional. Careful selection

is needed to ensure that barrier substances and protective clothing do not cause degeneration of this layer. The " mouth " of the follicle is covered by the same keratinous layer as that of the general skin. As the hair itself is also keratin, the barrier substance can bridge the gap between the hair and the skin. If a cream can be produced to give an effectively resilient film over the whole of the exposed part of the body, there appears to be no reason why a barrier substance should have to block the follicles to be effective when used in industry. This capacity and the resistant qualities of the film have been taken to be the main criteria of a successful barrier substance and on these principles a method of testing proprietary creams has been developed.

The tests so far proposed by others in no way simulate practical conditions. The Ministry of Labour and National Service Factory Department (1956) test, using the disintegration of a dried film in a solvent, is useful as a means of comparing creams, but since it uses a dried film, the results can in no way be correlated to practice. It also has the disadvantage that several of the recognized creams do not form films, or do so only with great difficulty. The methods produced by Sadler and Marriott (1946) have several good features. They fail in that they measure only the rate of penetration of the liquid through the film. In a large number of cases, very little irritant is required to come into contact with the skin to set up dermatitis. Thus the important factor is the time to penetrate and not the amount of penetration. The very important factor of film flexibility has been taken into account in neither of these tests nor in any others examined. The weakest point of most of the barrier creams tested has been the poor resilience of the film. It is impossible to avoid flexing the hand and consequently the barrier film. Where a cream has poor flexing properties, breaks must very rapidly appear in the film, which allows irritants to be pumped through these breaks on to the skin. It has been found in practice and in the tests to be described later that this pumping action is considerable. Any laboratory method for the evaluation of barrier cream must therefore take into account the flexing properties of a cream if results are to be correlated to practice.

In tests employing dyes as indicators of penetration, the use of expensive equipment is required to obtain accurate results, particularly in the method attributed to Grant in which penetration is recorded by the fluorescence caused by the wetting of Rhodamin 6 G. Sadler and Marriot developed a very similar method using the amount of red ink carried through a filter. Since both of these methods rely on increase in colour or fluorescence, a poor end point is obtained. Shaking with liquids has not been found satisfactory. There are too many variables in such a test to make it reliable, and widely varied results have been obtained by different experimenters. The only test suggested to me by the barrier-cream manufacturers has been a " water test ". The cream is applied to the hands in the normal way and the process against which the cream

is required to give protection is carried out. After a suitable interval, the hands are placed under cold running water. If the cream is still effective, it should, if designed for wet work, simply repel the water or if for dry work it should readily lather. The inadequacy of this test can be very simply demonstrated : if a small amount of trichlorethylene is poured on to the barrier cream, penetration is very rapid. This is easily felt by the stinging sensation on the hands. If the hands are then subjected to the water test, the result indicates that an unpenetrated film is still present.

The tests already proposed fail by over-simplification. It is impossible to take into account all the variables which are found in the practical use of barrier substances, the main being :

(i) The wide variation in skin types.

(ii) Flexion of the hands.

(iii) Acidity and alkalinity of sweat.

(iv) The range of surface temperature of the skin and air temperatures encountered.

(v) Variation in and combination of irritants.

(vi) The amount of grime, sharp objects and bacterial activity in the working surroundings.

Only mass practical trials could satisfactorily evaluate the effect of variations in skin structure and pH of sweat. Improvement in working conditions to reduce the incidence of dermatitis is a matter for the Factory Inspector and factory management. The three remaining factors can be evaluated by laboratory tests. A simple method for the evaluation of barrier substances has been developed which has been found to give results which agree very closely with the observations made in practice.

Investigations.

The Resilience of the Film of Barrier Substances.

Method.—The method is based on the " Maeser " type water-penetration tester for leather (Fig. 1). The movable arm A is pivoted about CD. The arm B is stationary. The movable arm is actuated by the eccentric E, which runs in this case at 60 r.p.m. The whole is powered by a small electric motor. The flexing time is one second. A 6 cm. square is drawn in the centre of a 9·0 cm. Whatman No. 50 filter paper and 0·42 g. of the cream under test is spread evenly over this area. This gives a film approximately 0·098 mm. (98 μ) thick, which is approximately $7\frac{1}{2}$ times that of the film which would be produced if the cream issued by the standard proprietary cream dispensers were to be spread evenly over an average man's hand. The amount used above has proved satisfactory in simulating practical conditions and in producing a film. With this amount of cream, it has been found that an evenly spread film can be obtained in the actual test area by simply spreading with the finger. The only source of error is faulty film formation. The film is tested by holding the filter paper against a bright light when any marked variation in film

thickness is readily seen. The apparatus can be set up for illumination from above or below. In practice, it is advisable to have both available so that the type most suitable for any given test can be used at the turn of a switch. In general, illumination from below by reflected light is the more useful, penetration being noted by the drop in optical density.

When a satisfactory film has been obtained, the paper is folded into a boat shape, the sides are held by paper clips and an excess of cream is applied outside the test

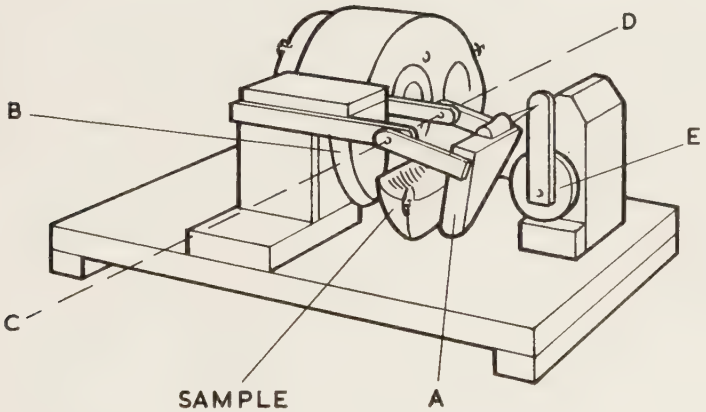

Fig. 1.

area to prevent the liquid under test from creeping on to untreated parts of the filter paper. The boat is then attached to the machine by means of " Sellotape " tags. One ml. of the liquid under test is applied by pipette to the boat. Thus only a small strip of the square is under test. The sample under test is kept as near as possible to 70° F.

Results.—The results obtained are set out in Table I and are expressed in minutes and seconds. The creams were divided into three groups for these tests, according to the recommendations of the makers on their suitability for protection against different types of irritants :

(i) Dry work : contact with dusts, oils, greases, petrol, paraffin etc.

(ii) Wet work : contact with water and water-based materials and organic solvents.

(iii) General work : contact with all materials whether dry or water-based and most organic solvents, paints etc.

The tests where " X " is recorded indicate that the sample ran for over 90 minutes without penetration, which suggests that it would last for a normal working period, assuming washing and replacement of the cream at tea or coffee breaks. The results expressed as " Z " were found to have an abnormally high degree of absorption and here the method was not applicable, thus no satisfactory results are available.

TABLE I.—*Results of Flexing Tests (Minutes and Seconds).*

Type of cream.	Sample.	Water.	Carbon tetra-chloride.	Tri-chlor-ethylene.	White spirit.	Paraffin.	Cod oil.	50/50 Sul-phonated cod oil/ water.	Old lime liquor.	Sod. sulphide 10% Aq.	Veg. tan. liquor (45° Bk.).	Chromic acid 10% Aq.	Basic chrome sulphite soln.	5% form-aldehyde soln.
Class I—Dry work	A	1′ 00″	1′ 30″	0′ 50″	2′ 00″	1′ 50″	37′ 00″	X	1′ 00″	12′ 00″	2′ 35″	0′ 50″	57′ 00″	1′ 50″
	B	1′ 2″	0′ 15″	0′ 10″	0′ 35″	1′ 00″	7′ 00″	52′ 00″	0′ 10″	0′ 20″	0′ 40″	0′ 10″	4′ 50″	0′ 45″
	C	Z	Z	Z	Z	Z	30′ 00″	X	X	X	1′—2′	5′ 00″	Z	0′ 20″
Class II—Wet work	D	1′ 00″	1′ 40″	3′ 20″	0′ 30″	1′ 35″	10′ 25″	4′ 00″	0′ 45″	8′ 00″	3′ 00″	0′ 15″	2′ 00″	1′ 60″
	E	2′ 3″	0′ 15″	0′ 06″	0′ 15″	5′ 50″	12′ 15″	X	17′ 00″	X	17′ 00″	20′ 00″	X	X
	F	Z	0′ 15″	0′ 10″	1′ 05″	0′ 10″	40′ 00″	X	4	3′ 30″	3′	0′ 40″	8′ 30″	4′
	G	1′ 40″	4′ 35″	8′ 40″	1′ 30″	4′ 00″	39′ 00″	3′ 15″	2′ 10″	X	7′ 00″	0′ 25″	1′ 10″	3′ 15″
	H	2′ 15″	0′ 30″	0′ 03″	0′ 05″	0′ 15″	0′ 35″	0′ 15″	29′ 00″	0′ 30″	0′ 15″	0′ 10″	0′ 40″	12′ 30″
Class III—General purpose	I	X	0′ 15″	0′ 10″	0′ 10″	0′ 15″	5′ 00″	X	X	6′ 90″	2′ 30″	2′ 45″	X	X
	J	10′	0′ 55″	8′ 00″	0′ 45″	15′	5′ 00″	40′ 00″	X	X	X	7′ 00″	30′ 00″	25′ 00″
	K	X	1′ 00″	0′ 15″	1′ 30″	3′ 00″	35′	X	20′	X	X	X	X	X

The pH of Barrier Substances.

The importance of a barrier substance having an approximately neutral pH is now firmly established. The following values were obtained with the creams used in this investigation :

TABLE II.

Cream.	pH.
A	7·5
B	7·5
C	8·5
D	8·0
E	8·0
F	6·0
G	7·5
H	8·0
I	7·5
J	6·0
K	7·5

The cream J at pH 6·0 had a very high buffer capacity and reduced the pH of a solution of sodium sulphide and saturated lime to neutral within 20 minutes. Sadler and Marriott state that such a cream would have very poor properties as a barrier, but as can be seen from the results in Table I, this cream had excellent barrier properties. It also had little blocking action on hair follicles and was extremely resilient. It has been shown (Brain, 1956) that triethanolamine, which is frequently used in barrier substances for the dual purpose of emulsification and buffering, is a primary irritant.

Protection Against Mineral Oil by Barrier Substances.

In view of the very poor results obtained in the flexing tests and the danger of oil acne from use of mineral oil, an investigation has been made into the makers' assertions that their products give adequate protection against mineral oil and facilitate its complete and easy removal from the skin.

Method.—The ability of mineral oils to fluoresce when subjected to ultra-violet light has been used as the basis for this test. I spread barrier substance over my hands in the normal way. A thin coating of raw mineral oil was then poured over the hands and they were flexed several times. The whole was then washed off. The time of contact was approximately $1\frac{1}{2}$–2 minutes. The hands were then washed three times with soap and warm water. In a large number of cases it took two washes to remove the barrier substance. Even after this exhaustive washing, a quantity of oil was left on the skin. The results are shown below and marks are awarded out of ten, thus the lower the value, the poorer the properties of the cream as a protection against mineral oil.

A control was carried out as above but without using a barrier substance and before washing, the hands were wiped with a clean dry cloth. On the above rating, the value would be about 8. It is apparent that the use of barrier substances alone is generally of no practical value as a protection against

TABLE III.—*Relative Value of Creams in Protection Against Mineral Oil.*

Cream.	Evaluation.
A	10
B	3
C	1
D	3
E	10
F	2
G	3
H	3
I	3
J	8
K	10

mineral oil. Their use is inadvisable for when workers are using such preparations they tend to wash less and will leave work quite happily with a fairly large amount of mineral oil held by the barrier substance blocking the hair follicles. A further disadvantage was found. The material in the follicle could not be removed except by very hard scrubbing, which in itself made the hands sore, and this is very liable to give rise to dermatitis. In efforts to remove this material and the oil/barrier mixture, ordinary hand soap, liquid soap, detergent, oil solvent and soap containing 5% sodium sulphite crystals were all tried but with very poor results. The simplest and most effective ways of removing the oil were found to be by the use of a mixture of neutral sulphonated castor oil and a wetting agent as recommended in " Oil Dermatitis ", Ministry of Labour and National Service publication No. 397 or by the use of the Borax Consolidated Limited product " Boraxo ". Provided the hands are suitably wet, this gives the required abrasive action to remove any material from the follicles without being harsh to the skin. Both these products have been found to be completely satisfactory whether or not a barrier cream has been used. Both products also leave the hands with a very pleasant feeling after use. The " Boraxo " also contains a soap which washes the hands at the same time. The use of a good after-work cleanser is therefore more useful than barrier substances in this particular field. When rags are used to remove oil from the skin, they must be clean rags and not dirty cotton waste, or this treatment is liable to be a source of dermatitis rather than a preventive.

DISCUSSION OF RESULTS.

Another useful method of assessing a barrier substance is to spread a barrier on to either the hand or a suitable type of leather. A vegetable-tanned sheepskin is satisfactory. If the latter method is used, a low power ($\times$ 32) binocular microscope is adequate but higher magnification is required for examining human skin. The resilience of the film is tested by scratching the surface with

a pin point or the blunt end of a piece of wire. This indicates the ability of the film to resist damage to the skin by sharp metal turnings, etc., which are so frequently the initial cause of dermatitis. In addition, it is possible to observe the nature and the extent of follicular blockage.

From the mineral-oil test and the observations made by microscopic examination, it appears that there is little or no connection between the degree of follicular blocking, the suitability of a barrier substance to resist oil and the ease of removal of both the oil and the barrier substance after work. In assessing the results reproduced in Table III, it must be remembered that these results were obtained only after exhaustive washing and drying. From my observations in carrying out these two tests, it appears quite certain that the main effect of a barrier substance in the prevention of skin contamination by mineral oil is produced by the film formed over the skin by the substance. It is not claimed that the reaction with sheepskin is identical to that of human skin but the reactions of mineral oils on human skin have followed very closely those prophesied from observations made on sheepskin.

In the four cases where the barrier substance was considered to be satisfactory in the short period under test, only creams A and E had any appreciable follicle-blocking properties as observed on sheepskin. In these creams, the filler particles appeared to be somewhat smaller than usual, which probably accounts for the ease of their removal. Cream J was not quite so satisfactory but it is thought to give reasonable protection. Here a slight amount of blocking was noted. In cream K there was no real blocking of the follicles but a resilient film was found to have formed over the surface of the follicles.

The microscopic technique is thought to be most useful in an assessment of a barrier substance for any type of work where loss of cream is liable to occur either by friction, "scratching" or displacement in any form. The film-forming properties and resilience of the films of several of the creams tested are strikingly poor.

A high degree of resilience in a cream adds much to the comfort of the wearer, which from a practical point of view is essential. Much has been written about the importance of the attractiveness of these preparations to the men or women in industry but little notice seems to have been taken of this by some manufacturers. Quite frequently, the cream remains sticky and uncomfortable on the hand for a considerable period after application, or for the whole time it feels like a tight-fitting glove. The odour of a barrier substance can be very important with women workers. I have had the experience of a perfectly good barrier being rejected due to its unpleasant smell. This is a small point, which the management is unlikely to take into account when choosing a barrier for use in its factory, but one which can encourage workers to use these preparations. As many barrier creams have a very pleasant feel and odour, it is unfortunate that other manufacturers do not modify their

preparations. From the present tests, I have found that these pleasant creams are no less effective.

Drying out of the cream when in use is undesirable and under general conditions unlikely. However, microscopic evaluations were carried out on films spread on to sheepskin and allowed to dry out. Creams C, D, G, and I were found to be very flaky and most of the cream was very easily lost. In the case of films E and F, although a certain amount of flakiness was observed, a flexible protective film was left over the surface. By scratch tests carried out on these films, B and H increased the amount of follicular blockage by the adhesion between the film and the filler. In the case of cream C, where there was a large amount of flakiness, the filler tended also to be pushed into the follicle. The remaining creams, A, B, H, J, K, all had satisfactory films even when allowed to dry out. In one particularly bad case, by simply flexing the leather once when the cream had dried out, 90% of the cream fell away in a powder.

From the flexing tests, it would appear that in general, barrier substances fall very far short of their supposed qualities and requirements. In the main, it seems that the creams J and K do in fact carry out their main function of being general purpose creams and at the same time exhibit properties equal to and in most cases superior to creams supposedly designed for specific irritants.

With regard to the four organic solvents tested, none of the barriers has a satisfactory resistance to any solvent. In relation to the solvents used in industry to-day, those chosen for testing are not the strongest, although some of the commonest with the exception of trichlorethylene which is well known to be dangerous. In this group, only creams G and J give reasonable protection : 8 minutes in the case of trichlorethylene and 15 minutes in the case of cream J with paraffin. The ridiculously low values obtained for protection against distilled water speak for themselves. It is most enlightening to note the very small difference between the creams for dry work and those for wet work with respect to the aqueous test.

The distressingly poor protection against chromic acid is alarming in view of the great danger to workers in the leather industry where this material is very frequently handled. With chromic acid, basic chromium sulphate solution (as used for tanning of chrome leathers) and formaldehyde solution (a liquor used for the treatment of fur-skins and leathers) the main cause of failure appeared to be reaction between the liquors and the constituents of the cream resulting in a loss of flexibility with the consequent breaks in the film. From the results obtained using saturated lime solution, sodium sulphide solution and vegetable tannin liquor, it would appear that in general resistance to alkalis is rather better than that to acid, the pH values of the respective liquors being approximately 12·0, 13·5, and 3·5.

In general, the results obtained are not very encouraging. It must, of course, be remembered that the values are for continuous contact with the irritant,

and practical values may in some cases be found to be slightly longer, although every effort was made in the formulation of this method to achieve results which would closely follow the results obtained in practice. It is of course, very difficult to determine when in practice the effectiveness of a barrier has worn off. Thus errors between practical use and laboratory tests are liable to occur. I feel that all these tests bear out my opinion, that in order to be in any way effective in practice, not only must a barrier cream be able to withstand breakdown and penetration of the film by the irritant, but the film must also have a very high degree of resilience in order to stand up to the normal movements of the hand and normal operations. Unless a barrier cream is resilient it will not withstand penetration by irritants.

Conclusions.

As commonly agreed by workers in the field of industrial dermatitis, the main deterrent to this plague is cleanliness. The provision of good washing facilities is accordingly essential in all factories. The abuse and lack of use of such facilities so frequently complained about by managements are in my experience, completely unnecessary and in the main due simply to bad management-worker relations. I have found that good washing facilities with a responsible person in charge are not abused and are also extremely good for the morale of the worker who generally makes full use of them. The upkeep of washplaces is frequently neglected, the commonest fault being the infrequent renewal of towels when wet and dirty. The use of dirty towels not only leads to general dirty habits amongst the workers but is also a major source of dermatitis. The use of paper towels is growing in industry to-day and with suitable supervision these have been found to be economical. Reports of their misuse for lunch wrappings etc., have been exaggerated and are unfounded in well managed wash-rooms. The use of roller towels is very unsatisfactory since these are replaced too infrequently and one part of the towel is used many times before renewal. Transfer of accumulated irritants from workers to towel and then to other workers must occur. The towel machines, most of which are available at a moderate hire rate, are much to be preferred as a good replacement service usually accompanies these machines and no part of the towel need be used more than once. The importance of good management relations and washing facilities cannot be too greatly stressed. In one tannery, 15 minutes are allowed at the end of the morning and afternoon shifts for the worker to wash and change. The facilities provide for good clean storage of clothing (most workers change their clothing before leaving the factory) and shower baths. The washrooms are maintained by one man and no experience of abuse or loss of interest has been experienced in several years. The cases of dermatitis have been negligible. Although it appears that the allowance of 30 minutes a

day for washing is rather high, in view of the facts that the time is allowed out of the working day and that the men are not allowed to leave before the end of the period, good health and good relations are effectively maintained.

The use of a good after-work cleanser is at all times to be desired whether or not a barrier substance is used. The necessity of testing a soap or cleanser prior to its general use in a factory has been shown by the results reproduced in Table III, and from the findings of Brain (1956) who found that washing with ordinary toilet soap raised the pH of the skin from 5·0 to 8·0 and that a lapse of 20 minutes occurred before the skin was back to its normal pH. As pH 8·0 has been stated to be dangerous, overwashing could lead to dermatitis or at least to a deterioration of skin condition. It has been suggested that the addition of a small amount of salt to the water used for washing can be very useful in minimizing this change in pH. Whilst it is felt that the many proprietary soapless and waterless hand-cleansing preparations may be very effective for cleansing industrially soiled hands, from personal experience of these materials, I believe that they tend to dry the skin and thus their use over a period of time may lead to degeneration of the skin and increased danger of dermatitis. If there is any danger of the removal of the natural greases from the skin, it is essential that an after-work cream is supplied to replace them. In general, these after-work creams consist of either lanolin or castor oil in a white vaseline base. The castor-oil creams seem more beneficial and faster acting than the lanolin creams. Care in the choice of this type of preparation is strongly recommended. I have found that some reputable varieties of this type of cream at present on the market are worse than useless, leaving the skin very greasy and unpleasant and having very little effect in restoring the skin to its natural condition. Unfortunately, the only way of assessing these creams is by their action on hands which have in some way been degreased. The action of some of the modern soap powders and detergents on the hands is efficient in the production of hands suitable for such tests.

Whilst good cleansing and reconditioning of the skin are at all times to be recommended, it seems more desirable to remove the cause of irritation than to have to reduce the effects or cure the results of these irritants. The removal of contact with the irritant can be brought about in several ways :

(i) Ensuring that clothing is kept clean and uncontaminated.
(ii) Adequate provision of efficient and well designed protective clothing.
(iii) Alteration of machinery and materials.
(iv) Provision wherever possible of mechanical means of handling.
(v) Installation of appliances to remove fumes and dust.
(vi) Sterilization of oil and materials used repeatedly.

Enlarging on these points, one of the main troubles arises out of the wearing of dirty overalls and other clothing (Whitwell, 1946). Trouble occurs especially

at the knees, thighs, collars and sleeves, where the clothing becomes impregnated with irritant and dirt, and rubs against the skin with the movements of the worker. The need for the renewal of worn clothing and the replacement and laundering of soiled articles at reasonable periods of time cannot be too greatly stressed.

The provision of protective clothing has long been recommended, but where such clothing is supplied it is frequently unsuitable for the operations which have to be carried out by the wearer. The chief fault here is the indiscriminate use of gloves. Short gloves are frequently the only gloves supplied and these leave the wrist and lower arm exposed to splashing. This leads to trouble in two ways. First, the worker very rarely treats these areas with barrier substance and this area is naturally less effective in resisting these materials due to the drop in thickness of the stratum corneum. Second, the irritant enters the glove and there is friction between the hand and the irritant-soaked face of the glove. The use of suitable gauntlet-type gloves is much to be preferred, but again there are several factors which can lead to increased danger. First, the right size and type of glove must be used for each operative. I have frequently found that gloves are supplied that are far too long for an operative to carry out the work required and he then simply turns down the top of the glove which becomes soaked in the irritant and is no more effective than wrist-length gloves. Second, the heat inside the gloves is generally much higher than in the shorter gloves with the ensuing effect on the protective layers of the skin. The development and use of mid-arm-length gloves which have tie-up tops would be better since they would eliminate the cone so frequently complained of as a collector of irritant and would also protect the clothing of the arm from becoming soiled. This type of glove would also reduce the amount of friction with the wide-topped gloves, the strengthened rim of which rubs the skin directly or through the sleeves of any garment worn beneath.

Industrial gloves made of rubber or more particularly of synthetic materials such as P.V.C. can lead to maceration of the skin and consequent dermatitis in warm conditions, even those of an English summer. Similarly, the wearing of the cheaper synthetic soling materials on shoes and boots leads to increased heat and sweating of the feet. This causes maceration of the soles of the feet and is probably the real cause of the increase of chrome dermatitis of the feet found to-day and not the increased use of chromium in the making of leathers for shoes as is generally suggested. This refers to the earlier and cheaper synthetic soling materials, not the newer types of foam rubbers and other vapour-porous materials which are now being used in the more expensive range of shoes, which although having a lower moisture-porosity rate than leather soling materials, should not lead to maceration with the normal person.

The relative advantage of using lined in preference to unlined gloves is debatable. Lined gloves which are put down by the worker soaked in perspiration and dirty through constant use are a greater danger than unlined gloves

unless the employer or wearer arranges for the laundering of these gloves or linings at reasonable intervals—most unusual in industry. The same applies where canvas and cotton gloves are worn, particularly as these are often provided for the handling of dangerous liquids without considering that this type of glove will absorb and retain any liquid with which it comes into contact.

A method of reducing the risk of dermatitis when wearing unlined gloves has long been stated to be the use of talc inside the gloves. Even when this is made available to employees at times other than during a visit of a Factory Inspector, with profuse sweating it does not prove very satisfactory and indeed can be quite uncomfortable to the worker after a while. In view of this, experiments with the use of barrier substances inside rubber gloves have been made. As a result of tests with several people who are known to have widely different reactions to barrier substances, it was found that in all cases when using a cream recommended for dry work with a high inert absorbent content, the results were most satisfactory and there was little discomfort to the wearer. These practical tests were of necessity on a small scale, but as there was a careful choice of test persons, they should be significant.

The improvement of materials and machines is to be desired wherever possible. The reports of the Factory Inspector have of recent years stressed most strongly the need for process-modification wherever possible to replace strong irritants with materials which are of less or no danger.

The provision of adequate splash guards on machines and the enforcement of their use are very great factors in this aspect of the prevention of dermatitis. The need for splash guards and similar appliances is further heightened by the findings of this investigation, as none of the creams tested resisted splashing by any of the materials used, complete and instantaneous penetration of the film occurring in every case.

From preliminary tests carried out with gelatin-liquefying bacteria, none of the creams tested appears to have any marked bacteriostatic or antiseptic properties. It is very desirable for them to have at least bacteriostatic properties, particularly with liquids which are recirculated, such as cutting fluids and other coolants, as these materials tend to have a high bacterial content due to contact with sores and expectoration by workers. It has been recommended (Forbes, 1943) that such liquids should be sterilized every fortnight by heating to 145° F. for a period of at least half an hour. A further source of danger occurs where tins of barrier creams are used in place of dispensers and the cream is contaminated by the workers. Care must always be taken with the addition of antiseptics as these may be irritant.

In many respects, the trade unions can be most helpful. I have met representatives of these bodies who have been most anxious to learn about and apply means for the prevention of dermatitis in their particular areas of jurisdiction. In the main, however, I have found trade union officials more

unco-operative than helpful in enforcing the use of the materials and precautions for their members' safeguard. This is frequently due not entirely to the trade unions themselves but arises, as do so many factors applying to the prevention of dermatitis, from bad management-union-worker relations. More tolerance on both sides and a willingness to examine local conditions and not to generalize will add greatly to an effective reduction in dermatitis in industry.

I do not feel at all competent to comment on the psychological effect and cause of dermatitis but the psychological effect of barrier cream has been examined by others with a wide range of operatives. The view has been expressed in medical literature that the provision of barrier substances reduces worry in the minds of a number of workers about the possibility of contracting dermatitis. Whilst it is impossible to disagree with this, it is my impression that a far greater number of people think of barrier substances as a means of reducing the time required or the necessity for washing at all after work and as such can be a potential source of danger and cause a great deal more harm than good.

Care should be taken in the choice of personnel where there is a risk of dermatitis. Age, previous working history, previous occurrence of industrial dermatitis or other skin ailments and mental stability should all be taken into consideration. This aspect has been very fully covered by Bettley (1954) and Hellier (1957).

The present tests have demonstrated quite conclusively that in the main the barrier substances marketed to-day do not give the degree of protection claimed by the makers. Where a degree of protection is afforded, it is unsatisfactory with the exception of the results recorded with an X in Table I. I have been most disturbed and puzzled by the attitude of the barrier cream manufacturers. In only one case was a manufacturer in any way co-operative although each was very ready to stress the complete infallibility of his products and to deprecate others.

I am still amazed by the results of the tests I have carried out and the odd way in which several of the creams have reacted in entirely the opposite way to that stated by their manufacturer. This is particularly true in the case of the mineral-oil test. In general, the " all-purpose " creams tested appear to be safer to use than the " wet " or " dry " type of cream, without a prior test of suitability. This fact, together with the lack of co-operation from the manufacturers, leaves me somewhat alarmed. This is further aggravated by the fact that none of the manufacturers approached will state what, if any, scientific tests are carried out on their products prior to their sale. One manufacturer did however inform me that a pilot-scale survey of the effectiveness of a new product on laboratory staff was the only test used.

When the writer began these investigations, he had in mind a scientific study to discover the barrier cream most suitable for the trade with which he is connected. He was aware of the recent literature and tests made condemning

the efficiency of barrier creams but he optimistically thought that this was due to unsatisfactory means of testing. Having completed an extensive range of tests he can but confirm the findings of earlier papers. Bearing in mind the unco-operativeness of the majority of makers with whom he has been in touch, he is forced to the conclusion that there is something drastically amiss in this particular industry. The writer is now of the opinion that the prevention of dermatitis must lie elsewhere than in the use of barrier substances unless drastic changes are made. It may be that the increasing use of silicones in barrier substances is the beginning of such a change.

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TRANSVAAL DERMATOLOGICAL SOCIETY

CASES SHOWN 1957–58.

? **Ocular and Cutaneous Angiomatosis.**—Dr. L. J. A. Loewenthal.

A woman aged 55.

Haemorrhages appeared in the right eye $2\frac{1}{2}$ years ago and shortly thereafter in the left eye. These led to glaucoma and both eyes were operated on by Professor Ehlers in Copenhagen. Dr. J. Graham Scott reports: "Both eyes are blind from cataract and presumably vitreous haemorrhage and possibly optic atrophy. The tension is normal but the iris of each eye presents posterior synechiae and many dilated blood vessels and the right eye has a small hyphaema."

Skin lesions began symmetrically on the extensor surfaces of the forearms and legs two years ago. They have not itched, but those on the lower legs have recently bled, then forming crusted ulcers.

Examination.—The extensor surfaces of both forearms and legs show numerous erythematous lichenoid papules and plaques, some confluent, of all sizes from 2 mm. to 1 cm. in diameter. They are slightly infiltrated and at first sight suggest psoriasis. However no scaling can be produced by light grattage. On the lower legs there are small deposits of recently dried blood and several shallow ulcers covered with adherent, bloody crusts. Neither purpura nor focal pigmentation are evident on diascopy and no telangiectases have been seen.

Histology.—Biopsy specimens from forearm and leg showed identical features. The skin is normal in every respect except for the presence of greatly dilated filled capillaries throughout the upper half of the corium. These vary in size from that of a normal capillary to the largest, which attain a diameter of about 150 μ; they are principally situated in the papillary layer, but accompany the pilo-sebaceous units to a depth of about 1·5 mm. All consist of a single layer of apparently normal endothelium; pericytes are not seen in excess of normal and there is no inflammatory reaction. Frozen sections stained for fat (Sudan III and Sudan black B) show lipaemia in the blood spaces but no other lipoid deposit.

Other investigations.—Urine—normal.

Blood—Hb 13·4; W.B.C. 9400 with normal distribution; platelets numerous. Total cholesterol 160 mgm%.

Comment.—The case appears to be one of *acquired angiomatosis* affecting the eyes and skin. No similar case has been found in the ophthalmological or dermatological literature.

Albinoidism with Epitheliomatosis.—Dr. L. J. A. Loewenthal.

A woman aged 40.

History.—This patient inherits, through her mother, the condition of albinoidism. This appears sometimes as a white "blaze" in the scalp hair, sometimes as patches of leucoderma, or in some members of the family as both. Her two children, like the patient, have leucoderma of the legs.

About 13 years ago a psoriasiform lesion developed in an albinotic patch on the left leg. This was treated with x-ray in 1953. Since then two further patches have appeared in the same albinotic area. Six years ago a similar lesion appeared on the left lower eyelid and was treated with x-ray.

Histology (recent lesion of leg).—Intra-epidermal epithelioma.

Comment.—Although the patient is of the sandy-haired, freckled type, who develop cutaneous neoplasms so readily here, it is interesting to observe that three of these growths have appeared in an albinotic patch. She is actually so fair-skinned that the albinotic patches can be made out only with difficulty.

? Teleangiectasie Essentielle en Plaque of Brocq (Acquired Type) ? Telangiectatic Lupus Erythematosus.—Dr. G. H. Findlay and Dr. L. J. A. Loewenthal.

Case 1.—A woman aged 36.

History.—About 8 years ago she first noticed a redness, only on the left cheek : this later spread to the neck, forehead and left upper chest and over the front of the neck. In September 1956 a spot on the right cheek was also noticed. Chloroquine and mepacrine have had no effect. In 1956 some swelling of the spots with a little surface scaling was noted : this swelling was intermittent and sometimes looks urticarial.

Suffers with a spastic colon and constipation.

Case 2.—A woman aged 30.

History.—Blotchiness noted on the left side of the face 6 years ago. Itching and burning occasionally. Frequently treated with chloroquine without benefit. Suffers with a spastic colon and constipation.

Examination.—Erythema with telangiectases, roughly in distribution of left maxillary division of 5th nerve. A few telangiectatic spots on right side also.

Histology.—Both cases show the same features : slight vacuolation of cells in the basal layer, dilatation of capillaries in the upper corium, and massive perivascular cellular (chiefly lymphocytic) infiltrate in the middle third of the corium.

Hyalinosis Cutis.—Dr. G. H. Findlay.

A male storeman aged 19.

Since the age of 8, this patient has had repeated swelling and burning of the hands that subsides after a few days, with temporary discoloration and permanent wrinkling. The skin on the face and hands is tender. Heat and sunlight cause subjective burning. One episode of a tense purpuric oedema has been seen similar to these attacks which have occurred a few times every year since the onset. Seven sibs and all known relatives were considered normal.

On examination the hands resemble the elastotic hands of an elderly labourer. The face is pale and sclerotic, with a vermiculate atrophy. Intellectually he is slow and perseverating, with labile moods.

Punch biopsies were done painlessly without local anaesthesia. Histologically both the hands and face showed the hyaline changes as seen in lipoid proteinosis. No fat was demonstrated in frozen sections stained with Sudan III.

Gamma globulins and sedimentation rate were slightly raised. Serum mucoproteins, blood count and liver functions were normal.

Comment.—This patient is regarded as an abortive example of lipoid proteinosis, without clinical involvement of the mucosae : no lipoid demonstrable with Sudan III in one specimen, and a negative family history.

Radiodermatitis Presenting with Nail Changes. Dr. C. M. Ross.

A General Practitioner aged 32.

This patient's first symptoms were discoloration and friability of the nails of his left index and middle fingers. These appeared in September 1956. Shortly afterwards he was told he had a fungus infection of the nails, though no microscopic or cultural investigations were done. He was given two doses of radiotherapy to the nails themselves, the fingers being protected with lead.

When I first saw him in November 1957, the nails were crumbling at their free edge and the nail plates were brown, opaque and striated. The skin on the dorsal surface of the middle and distal phalanges showed some mottled bluish discoloration. An x-ray reaction was considered unlikely because of the shortness of time since his radiotherapy, the small dosage used and the protective measures adopted. A culture was taken from the nails and *Candida krusei* was isolated ; he was advised to file down the nails, to apply Nystatin ointment and to take Nystatin by mouth. There was no improvement.

During the course of discussion at the Meeting, in which he himself took part, the patient revealed for the first time that during the previous five years he had, in the course of his practice, screened many of his patients and x-rayed them for fractures without protecting his hands.

A biopsy was taken from the affected skin and showed changes compatible with radiodermatitis. In the three months which have elasped since the meeting, the skin on all the fingers of the left hand and on two of those on the right hand has become dry, scaly and telangiectatic and a small crusted erosion has developed on the left middle finger.

The patient has now been referred for plastic surgery.

His case is described as a timely warning to us all.

Congenital Mastocytosis. Dr. L. J. A. Loewenthal.

A girl aged 6 months.

At the age of 2 months yellow flecks appeared on the body, became bigger and more numerous. Some have blistered spontaneously. Attacks of *flushing* have also occurred, first infrequently, but later daily. The flush begins on the face, then involves the neck, shoulders, upper arms and trunk ; it lasts about 20 minutes and the child appears to be restless and distressed. No precipitating factor has been noticed.

Examination.—Numerous macular, fawn coloured lesions are present on the head, trunk and limbs. Some show recent bullae. Varying degrees of urtication can be produced by rubbing, some spots reacting more readily than others ; no generalized flush observed after rubbing the lesions. No other physical abnormalities found.

Urine was collected after a flushing attack and examined for 5-hydroxy-indole-acetic acid, with negative results.

Biopsy was not made.

BOOK REVIEWS.

The Medico-Chirurgical Encyclopaedia.*

This volume contains a review on classical lines of erythemato-squamous dermatoses including a survey of parapsoriasis, another on erosions, ulcerations and gangrene and an account of dermatological surgery which contains some useful points for the dermatologist. Minor articles deal among other things with decubitus ulcers, lethal bullous ichthyosiform erythrodermia and ocular pemphigus though there is no reference to British contributions on the latter subject. F. F. H.

The French Atlas.

XVIIth Section.

The text of this section deals mainly with metabolic disorders and with leishmaniasis and yaws. In their introductory note the authors mention that tropical diseases are becoming more common in France owing to the greater movement of populations and this, of course, is a tendency which we see in the United Kingdom to-day.

The text on the xanthoma group constitutes a very useful summary, well documented, on this whole group of disorders.

It is not easy to judge the adequacy of some of the illustrations because one is aware that further illustrations may be in store in succeeding sections. Thus primary amyloidosis is illustrated by pictures which are not the most typical; the pictures of bromoderma are not up to standard and the one picture of yaws is not particularly helpful. No doubt, however, there will be more pictures later on which will complete these subjects. This section also contains one picture of necrobiosis lipoidica which is one of the best pictures so far to have appeared in the Atlas. F. R. B.

Clinical Calorimetry.†

This monograph deals in detail with methods of measuring and recording skin and tissue temperature. Interesting graphs of the temperature usually obtaining in various sites on the body surface, and within the body cavities, are to be found. The physical aspects of temperature measurements, with regard to ambient temperatures, together with biological considerations are fully explained, and the technique of heat flow studies by means of calorimetry is described. There is a useful section on electrical equipment, and circuit diagrams are shown. A series of thermocouples of various shapes and material is listed and suggestions are made as to the best for use in particular circumstances. The use of temperature studies in peripheral circulatory disorders, experimental pharmacology, and controlled hypothermia, is discussed.

Research workers contemplating the use of these methods would do well to consult this work where much help can be obtained in the choice of apparatus, and in methods of procedure. M. G.

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* *Encyclopédie Médico-Chirurgicale : Recueil Periodique.* (1958) No. 14. Paris: Editions Techniques.

† *Klinische Calorimetrie und Thermometrie.* Helmut P. Kuemmerle (1958). Stuttgart: Georg Thieme Verlag. Pp. 112.

Tropical Dermatology.*

This book, which covers the dermatological field very fully in note form, should prove useful to students and practitioners in tropical countries. Each condition that is considered is described in short paragraphs on aetiology, incidence, signs and symptoms, diagnosis, prognosis and treatment, which makes for easy reference. The spelling requires much editing (e.g. grnuloma inguanle and pseudobobo on p. 240) and a number of the photographs are not instructive and could well be left out.

Nevertheless this book contains much information on tropical dermatology.

S. T. A.

Pediatric Dermatology.†

This is a comprehensive account of skin diseases occurring in infancy and childhood. Many diseases usually considered to be confined to adults are described or, at least, mentioned. Chapters on the anatomy and physiology of the skin and general principles of treatment and diagnosis are included, so that this work might almost serve as a text-book of general dermatology for the post-graduate student. The general principles and details of treatment are excellently presented and, indeed, throughout the book there is a refreshing and commonsense approach to dermatological problems. Ideas and beliefs based on less than adequate evidence are discarded.

It is difficult to agree with the author's statement that a good therapist need not necessarily be a particularly good diagnostician—undiagnosed scabies in infants is not often treated with any degree of success.

The importance of allergic contact eczema in children is perhaps over-stressed but the reviewer agrees so completely with Dr. Leider's views on atopic eczema that it is almost embarrassing to praise them. The difference between the appearance of certain skin disorders in adults and in children is not always sufficiently emphasized. An example of this is the section on dermatitis herpetiformis in which the adult form of the disease is described although there is an excellent illustration of the juvenile variety.

Dr. Leider is to be congratulated upon the amount of useful information he has included, and particularly upon the readable way he presents it.

R. H. M.

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* *A Treatise on Tropical Skin Diseases.* K. D. Lahiri (1956). Calcutta : Thacker, Spink & Co. (1933) Private Ltd. Pp. 359. Illus. 209. Price 12 Rupees.

†*Practical Pediatric Dermatology.* Morris Leider (1956). St. Louis : The C. V. Mosby Company. Pp. 433, 280 photographs and 13 drawings. Price 78*s.* 6*d.*

CURRENT LITERATURE.

SENSITIZING STRUCTURE IN EPOXY RESIN. L. E. Gaul. (1957) *J. invest. Derm.*, **29**, 311.

Uncured or merely aircured epoxy resins can be powerful sensitizers. The allergenic factor resides in the bisphenol part of the molecule and not, it appears, in the epoxy group. The patient concerned gave positive patch tests to 0·001% of the uncured resin in olive oil but failed to react to it after it had been heat cured. J. H. T. D.

EFFECT OF ADRENOCORTICAL STEROIDS ON CYSTIC AND PAPULAR ACNE. J. L. Danto. (1957) *J. invest. Derm.*, **29**, 315.

A modest daily dose of cortisone, 75–100 mg.—almost enough to cure pemphigus when it was a new drug—now restores that school-girl complexion. The good effect is attributed to the " anti-inflammatory property of the hormone and/or to the temporary suppression of the secretion of the pituitary gland ". J. H. T. D.

THE TONOFIBRILS OF THE HUMAN EPIDERMIS. A. Charles and F. G. Smiddy. (1957) *J. invest. Derm.*, **29**, 327.

Electron microscopy adds to our knowledge of the structure and function of the tonofibril. J. H. T. D.

PHOTO-ALLERGY AND PHOTO-CROSS-SENSITIVITY TO PHENERGAN. S. Epstein and R. J. Rowe. (1957) *J. invest. Derm.*, **29**, 319.

The patient whose case gave rise to these speculations had continued for 6 months to ingest phenergan originally prescribed in the treatment of suspected poison-ivy dermatitis. Not only did he have a chronic eczematoid dermatitis of all exposed parts but at least 3 weeks after stopping the treatment his skin continued to give a strong sunburn reaction to quite feeble doses of U.V.L.

The term photo-allergy implies that the skin reacts abnormally to light because it contains the drug, harmless in this respect to most people, or some oxidation or metabolic product which may persist in the skin long after the drug has been excreted. Phototoxicity refers to non-allergic phenomena which can be produced at will in man or animals " e.g. if an adequate dose of sulphanilamide is injected intradermally every tested person will respond with an increased sunburn reaction at the site of injection ".

Photo contact sensitivity implies an eczematoid reaction or an aggravation of such reaction by light in test sites in patients who may or may not have given an ordinary positive patch test to the drug. J. H. T. D.

STUDIES ON CHOLESTEROL AND CHOLESTEROL ESTERS IN SKIN SURFACE FATS. Dorothy B. Windhorst and Roscoe C. Foster. (1957) *J. invest. Derm.*, **29**, 339.

There is not much variation in the esterified sterol content of the grease from the glabrous skin of different subjects but in the ratio of free to esterified sterols there is just enough difference in material obtained from prepubertal boys, matrons, followers of Esau and of Elisha, in that order, to support the hypothesis that cholesterol is a by-product of keratinization—perhaps of the hairshaft. J. H. T. D.

THE SENSORY END-ORGAN OF THE HAIRLESS SKIN OF THE CAT. R. K. Winkelmann. (1957) *J. invest. Derm.*, **29**, 347.

Man has 3 kinds of end organ: mucocutaneous, Meissner-Merkel and Vater-Pacini; the cat has only 2, one of which does indifferently for sides of tongue semi-mucosae and foot-pads, and is here described. J. H. T. D.

THE EFFECT OF SEVERAL SUBSTANCES ON THE KERATINIZATION OF THE RAT EPIDERMIS. E. O. Butcher. (1957) *J. invest. Derm.*, **29**, 377.

Local treatment with linoleic and oleic acid causes hypertrophy of the rete and parakeratosis. 5% alkyl aryl sulphonate accelerates keratinization. Sodium selenite does the same but also

inhibits growth and would, according to the not very clear microphotographs, appear to do considerable damage. Sodium selenate and sodium tellurite had similar but slighter effect, arsenic trioxide and molybdenum (the salt not mentioned) none. J. H. T. D.

LONG-TERM TISSUE CULTURE OF EPITHELIAL-LIKE CELLS FROM HUMAN SKIN. C. E. Wheeler, C. M. Canby and E. P. Cawley. (1957) *J. invest. Derm.*, **29**, 383.

The attempt to prepare a tissue culture of epidermis failed in all but one of 10 attempts. This concerned a Thiersch graft from the buttock of a 17-year-old boy.

After 3 days in the refrigerator 4–6 sq. mm. pieces of epidermis separated by trypsin were sown in 40% human serum, 5% chick embryo extract, which had been carefully frozen, thawed and filtered. Thirty-one days later a small colony appeared in one of the tubes and presently began to multiply rapidly and to develop characters similar to the HeLa strain, not a little suggestive of malignancy. The culture was quite efficient for the propagation of herpes simplex virus.

J. H. T. D.

LOCATION OF THE SUPERFICIAL EPITHELIAL BARRIER TO SKIN PENETRATION. S. Monash. (1957) *J. invest. Derm.*, **29**, 367.

That the whole of the horny layer, as opposed to the stratum lucidum alone, must be taken into account when considering its permeability by anti-histaminics and local anaesthetics, is suggested by these experiments with scotch tape. It takes 600 strippings to remove the 98% of the horny layer of the palm that is required to permit absorption of a local anaesthetic.

J. H. T. D.

THE BEHAVIOUR OF HUMAN SKIN, ITS APPENDAGES AND TUMOURS IN HETEROLOGOUS HOSTS. G. W. Hambrick and Rosalyn Bloomberg. (1957) *J. invest. Derm.*, **29**, 353.

A suspension in penicillin saline of minced tissue was injected into the submucosa of a hamster's pouch. Two months or more may elapse before heterograft reaction destroys it.

Foetal epidermis proliferated to some extent and differentiated within about 3 weeks into adult covering epithelium and appendages, surviving altogether for 90 days. Tumours behaved like adult skin. The ability to survive did not seem to depend on the presence of glycogen.

J. H. T. D.

PROTEOLYTIC ACTIVITY IN DERMATOSES : PRELIMINARY OBSERVATIONS ON INFLAMMATION AND PRURITUS. F. E. Cormia, J. W. Dougherty and Shirley A. Unrau. (1957) *J. invest. Derm.*, **29**, 425.

Whereas itching provoked by histamine is always accompanied by a visible reaction, the injection of trypsin may produce itching without such reaction and even after the itch response has already been exhausted by histamine.

Though the intradermal injection of proteolytic enzymes will aggravate an inflammatory lesion it produces less itching than in undamaged skin.

The pruritus sine materia of uraemia, hepatitis, lymphoblastoma and certain emotional disorders may well be mediated by circulating proteolysins. J. H. T. D.

EFFECT OF PERCUTANEOUS ABSORPTION OF METICORTELONE ON THE EOSINOPHILE COUNT. D. N. Tschan and L. Adon. (1957) *J. invest. Derm.*, **29**, 385.

Inunction of one-quarter of the cutaneous surface with 0·5% meticortelone ointment resulted in a fall in the eosinophil count after 4 hours in 9 out of 10 patients having 100 or so eosinophils per cubic millimetre of blood. J. H. T. D.

THE RELATIONSHIP BETWEEN SKIN HYDRATION AND THE SUPPRESSION OF SWEATING. W. C. Randall and C. N. Peiss. (1957) *J. invest. Derm.*, **29**, 435.

THE EFFECT OF VAPOR IMPERMEABLE GLOVES ON EVAPORATION AND SWEAT SUPPRESSION IN THE HAND. C. N. Peiss and W. C. Randall. (1957) *J. invest. Derm.*, **29**, 443.

Exposure of the skin to water or to sweat inside a rubber glove results in maceration, poral closure and suppression of sweating. Reduction of the vapour pressure by cold or reversal of the osmotic gradient by adding salt to the water prevents this reaction, which in any case is quickly reversed when the normal state of the horny layer has been restored by evaporation.

J. H. T. D.

SENSITIVITY AND SPECIFICITY OF REITER PROTEIN COMPLEMENT-FIXATION (RPCF) TEST FOR SYPHILIS. C. R. Rein, Louise C. Kelcec, G. D'Alessandro and J. H. De Bruijn. (1957) *J. invest. Derm.*, **29**, 459.

A series of 1055 sera, submitted to a comparison of non-treponemal C. F. tests with tests employing antigens derived from virulent *Treponema pallidum* and from the non-pathogenic Reiter treponema, provides substantial evidence in favour of the latter. J. H. T. D.

TOPICAL APPLICATION OF MORE SOLUBLE FORMS OF HYDROCORTISONE. A COMPARISON WITH HYDROCORTISONE ACETATE AND HYDROCORTISONE (FREE ALCOHOL). C. C. Smith. (1957) *J. invest. Derm.*, **29**, 455.

The water-soluble forms of hydrocortisone employed in this study were found to be less effective than the standard forms with which they were matched in simultaneous paired comparison. That both were found so infrequently to be equally ineffective underlines the lack of a dummy control. J. H. T. D.

ISOLATION OF MICROSPORUM DISTORTUM FROM ANIMALS IN THE UNITED STATES. W. Kaplan, Lucille K. Georg, S. L. Hendricks and R. A. Leeper. (1957) *J. invest. Derm.*, **29**, 449.

The physical malformations of this microbe imported with pet monkeys from Nicaragua does not handicap it in its search for mammalian nourishment. J. H. T. D.

SCLERODERMA (ACROSCLEROSIS). I. TREATMENT OF THREE CASES OF THE NON-CALCIFIC VARIETY BY CHELATION (EDTA). J. G. Rukavina, C. Mendelson, J. M. Price, R. R. Brown and S. A. M. Johnson. (1957) *J. invest. Derm.*, **29**, 273.

SCLERODERMA (ACROSCLEROSIS). II. TRYPTOPHAN METABOLISM BEFORE AND DURING TREATMENT BY CHELATION (EDTA). J. M. Price, R. R. Brown, J. G. Rukavina, C. Mendelson and S. A. M. Johnson. (1957) *J. invest. Derm.*, **29**, 289.

Three cases of non-calcifying scleroderma were found to have abnormal tryptophane metabolism manifested by an abnormally heavy excretion of kynurenine and related substances. Excretion of these substances was suspended by disodium ethylene diamine tetra-acetic acid alone in 2 cases and combined with pyrodoxine in the third. It is supposed that chelation lowers the tissue calcium and releases magnesium from some other combination making it possible for the metallic ions normally interacting with pyridoxal phosphate to be utilized more advantageously.

The patients were treated by slow intravenous infusion of 500 c.c. of 5% aqueous solution of glucose containing Na_2 EDTA at a dosage of 50 mg. per kilo per diem for 3 weeks at a time. There appears to be little danger of tetany or of decalcification; and the side effects reported were banal and not out of proportion with the clinical improvement.

The metabolism of tryptophane, calcium and magnesium and the possible influence of trace metals on the pathology of the connective tissues are treated in great detail; and reference is made to no less than 127 authorities. J. H. T. D.

THE PENETRATION OF AN ANTICHOLINESTERASE AGENT (SARIN) INTO SKIN. I. RATE OF PENETRATION INTO EXCISED HUMAN SKIN. I. H. Blank, R. D. Griesemer and E. Gould. (1957) *J. invest. Derm.*, **29**, 299.

A piece of skin, obtained at operation or between 4 and 24 hours after death, is tested for adventitious permeability by placing it between 16 mm. electrodes at a potential of 1 volt and discarding it if it should pass more than about 1 microampere. The epidermal surface may be stripped to any desired extent with scotch tape, after which the piece of skin is made to form the diaphragm of a cell capable of being hermetically sealed at the end containing the substance to be tested and of housing some device to conserve moisture at the other. When diffusion has proceeded at the temperature selected and for the time desired, the cap is removed and the substance washed off. A piece 15 mm. in diameter is then punched out, the epidermis separated by immersion in water at 60° C., and to exclude mechanical contamination by the punch or leaching during separation, the disc of dermis is again trimmed by means of a 1 cm. punch, frozen and ground.

If the substance under test has been synthesized with an isotope (in this case P^{32}) the piece of dermis can be digested with nitric acid; otherwise the ground dermis is extracted with water and the supernatant assayed by a colorimetric method that is available for this particular purpose. J. H. T. D.